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Acute Renal Cortical Necrosis

Variable Course and Changing Prognosis

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Three cases of acute bilateral renal cortical necrosis, each with a different clinical course, are discussed. One patient spontaneously recovered renal function after prolonged oliguria. This case should be added to the small number of similar case reports in the literature. The second patient recovered adequate renal function temporarily, but eventually required chronic hemodialysis and renal transplantation. There was pathological evidence of progression from focal to massive cortical necrosis. The third patient never regained renal function, but is well after dialysis and transplantation.

The influence of modern theories of pathogenesis of the disease, and increased availability of dialysis, are discussed in relation to the initial prognostic assessment of the patient with cortical necrosis.

RENAL CORTICAL NECROSIS has been studied extensively since it was first described by Juhel-Renoy in 1886. It occurs most frequently following a complication of pregnancy,[1-3] particularly abruptio placentae.[2-4] Other precipitating events of an obstetrical nature are toxemia of pregnancy, retention of a stillborn fetus, and septic abortion.[2,3] The most common non-obstetrical cause in adults is sepsis.[2,5] Other causes are burns, shock, and neoplasm.[5] Cortical necrosis was the cause of approximately 2 percent of all cases of acute renal failure in a large series.[6]

The most characteristic clinical feature of the disease is anuria. Flank pain, gross hematuria, fever, severe anemia and hypotension have also been observed.[5] Calcification of the cortex is an occasional radiologic finding.[7] The usual course of severe cases, particularly in earlier studies, was progression to terminal renal failure.[1-4,7] Recovery of renal function following prolonged oliguria is rare.[1,9-11] One such case is presented herein; and in two other cases the patients are living and well following hemodialysis and transplantation.

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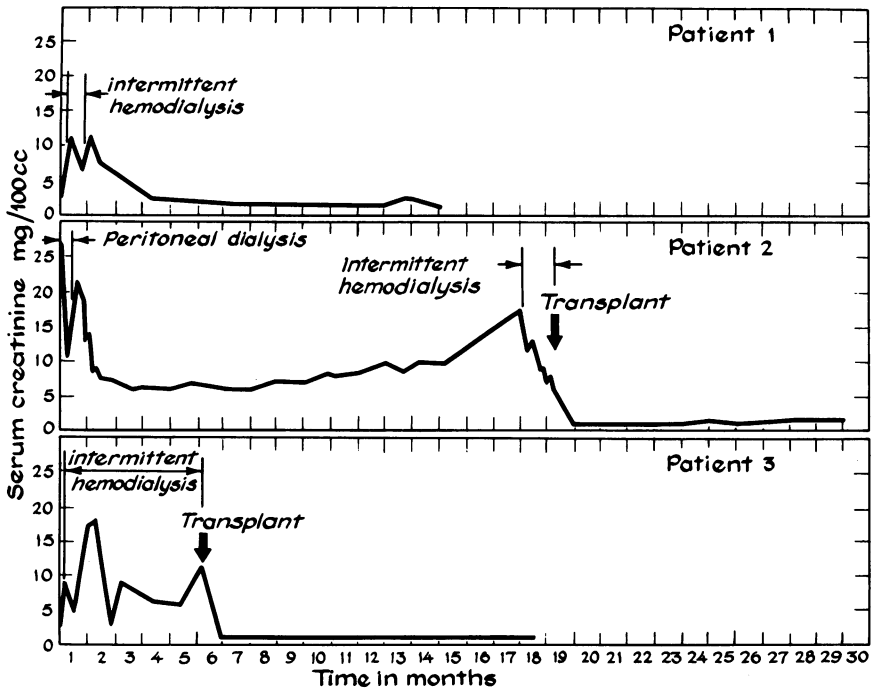

Chart 1.—The clinical course of each patient as reflected by the serum creatinine. Note the spontaneous and persistent improvement of Patient 1, the temporary improvement and later deterioration of Patient 2, and the absence of any spontaneous improvement of Patient 3.

Summaries of Cases

Patient 1. A 28-year-old multipara in her eighth week of pregnancy entered Stanford University Hospital for an elective saline-induced abortion 5 August 1969. She said she had not had previous renal disease and hypertension. Blood pressure and urinalysis on admission were within normal limits. Immediately following the abortion the patient became anuric. Profuse vaginal hemorrhage was treated by uterine curettage, fibrinogen, and transfusions of whole blood. Several hours after the operation the prothrombin time was 27 percent, partial thromboplastin time 75 seconds, fibrinogen 70 mg per 100 ml, and the platelet count 80,000 per cu mm. Microangiopathic changes were noted on a peripheral blood smear. Disseminated intravascular coagulation secondary to amniotic fluid embolism was suspected, and heparin therapy was begun. On the following day the patient was dyspneic; she complained of flank and left anterior chest pain. The blood pressure was 86/64 mm of mercury. Bilateral costovertebral angle tenderness was noted, as was diffuse ecchymosis. She remained anuric. The serum creatinine was 3 mg per 100 ml. The urine was grossly bloody and the protein content 3+. The sediment contained innumerable red blood cells, a moderate number of renal tubular epithelial cells, and a few granular casts. No hemoglobin casts were seen. On the basis of the clinical evidence, acute cortical necrosis was felt to be the most likely diagnosis.

By the third day of illness the fibrinogen level, partial thromboplastin time and prothrombin time had returned to normal. Heparin was discontinued. By the fourth day symptoms had disappeared and blood pressure had returned to normal. During the next two weeks the hematocrit dropped gradually from 29 percent to 18 percent. It returned to 26 percent (without transfusion) by the time of discharge on the 12th day. Anuria persisted and hemodialysis was required. The ecchymosis cleared.

On the 24th day of illness, urine output increased and dialysis was discontinued. The serum creatinine decreased from 11.1 mg per 100 ml on that day to 2.1 mg on the 100th postoperative day (Chart 1).

One year later the patient was asymptomatic, and physical examination was normal. The hematocrit was 36 percent and a peripheral blood smear normal. The blood urea nitrogen (BUN) was 30 mg and the serum creatinine 1.7 mg per 100 ml. Nephrotomograms revealed kidneys 11.5 cm in length without calcification. Examination of kidney tissue obtained by percutaneous biopsy revealed that a band of fibrous tissue had replaced most of the cortex; however, the remaining glomeruli appeared normal. These findings were interpreted as representing healed cortical necrosis.

Two years following operation the patient was

still asymptomatic and serum creatinine was 1.1 mg per 100 ml.

Comment

The initial clinical manifestations of this case of cortical necrosis were fever, gross hematuria, flank pain and anuria. The hypoprothrombinemia, thrombocytopenia, and microangiopathic hemolytic anemia were consistent with disseminated intravascular coagulation, possibly precipitated by an amniotic fluid emolism. A long period of anuria ensued. Although renal biopsy was not performed during the acute episode, the histologic features one year later were entirely consistent with previous acute cortical necrosis. The contribution of heparin to the successful management of this patient is conjectural, although previous studies have suggested a beneficial effect of heparin therapy in disseminated intravascular coagulation and related syndromes.[9,12] The limitations of percutaneous biopsy in establishing the diagnosis and the extent of acute cortical necrosis are demonstrated by this case. Had the biopsy specimen contained only fibrous tissue, complete cortical destruction might have been suspected. If it had contained only normal glomeruli, the diagnosis could not have been established.

Patient 2. A 17-year-old girl was first admitted to Stanford University Hospital in acute renal failure in January 1969. She had been quite healthy until three weeks before admission, when she experienced chills, fever, mild sore throat and periumbilical cramps. Weakness, nausea, and vomiting prompted her to consult a physician two days before admission. During the three days before she entered the hospital she was oliguric.

On 5 January 1969, a seizure prompted admittance to hospital. On arrival, she was somnolent and had generalized hyperreflexia. The blood pressure was 128/84 mm of mercury. The fundi were normal and there were no petechiae. A grade 3/6 apical systolic murmur was present. The hematocrit was 26 percent. The urine sediment contained 10 to 15 erythrocytes and leukocytes per high-power field, occasional oval fat bodies and finely granular casts. The serum creatinine was 28 mg per 100 ml and the BUN 255 mg per 100 ml. The ASO titer was 166 Todd Units. The platelet count, prothrombin time, clot retraction and bleeding time were within normal limits. A lupus erythematosus preparation was negative.

Peritoneal dialysis was instituted and somnolence disappeared. The daily urine output was less than 70 ml for four days. A low-grade fever persisted for four days. Dialysis was discontinued five days after admission. The next day the urine output began to climb steadily. Serum creatinine reached a high of 20.4 mg per 100 ml, then gradually decreased to 6.3 mg at the time of discharge, two months after admission (Chart 1).

Nephrotomograms done one week after admission demonstrated approximately normal renal size. The right kidney was 12.4 cm long and the left kidney 13.7 cm. A repeat examination six weeks later showed bilateral decrease in length, to 9.5 and 10.0 cm. There was no calcification.

Open renal biopsy was performed during the eighth week of illness. Microscopic examination showed extensive areas in which all the glomeruli were hyalinized or necrotic, and all the tubules either were replaced by fibrous tissue or showed acute and chronic inflammatory cell invasion. Elsewhere the tubules were hypertrophied and the glomeruli exhibited focal basement membrane thickening, with focal proliferative and necrotizing changes. These changes were interpreted as representing focal cortical necrosis.

Following discharge of the patient, renal function remained stable for nine months, but then began to deteriorate; by the 17th month the serum creatinine had risen to 17.1 mg per 100 ml (Chart 1). During this period several urine cultures and lupus erythematosus preparations were negative. During the 17th month chronic hemodialysis was begun.

Bilateral nephrectomy and splenectomy were performed during the 19th month. Renal sections were typical of massive cortical necrosis (Figure 1). Only a very thin rim of cortex was present, with hyalinized, closely packed glomeruli (Figure 2). In the remainder of the kidney interstitial fibrosis, tubular atrophy and dilatation, and foci of chronic inflammation were observed. Twenty months after the onset of illness the patient received a renal transplant with her father as donor. During 14 months of observation after transplantation she has been free of symptoms, and results of physical examination were always within normal limits. Serum creatinine was 1.1 mg per 100 ml, and the creatinine clearance 54 ml per minute.

Comment

The findings on renal biopsy early in the patient's course were compatible with focal cortical necrosis. When the kidneys were removed 18

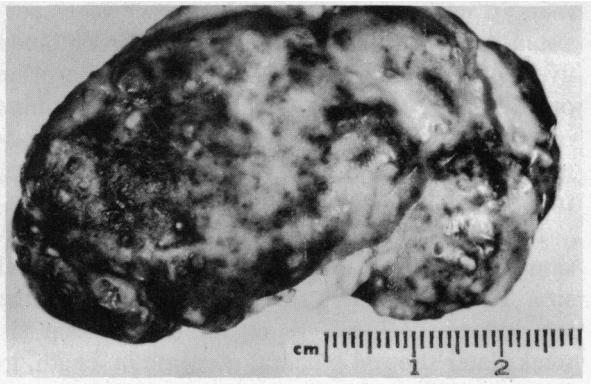

Figure 1.—Nephrectomy specimen (Patient 2).

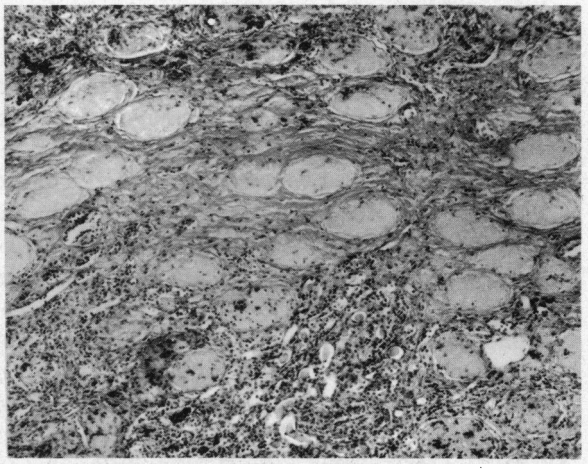

Figure 2.—This portion of the nephrectomy specimen is a subcapsular cortical area with total glomerular hyalinization and tubular loss. Note the inflammatory infiltrate at the edges of this area (Patient 2).

months later the findings were typical of the massive or "gross" form of the disease. The cause of the cortical necrosis is obscure. Progressive renal failure following partial recovery of renal function has been reported in acute cortical necrosis,[9,15] but has never been adequately explained. In this case there was pathological documentation of progression from focal to massive cortical necrosis, although there was no evidence of chronic disseminated intravascular coagulation.

Patient 3. A 39-year-old woman experienced severe vaginal bleeding and abdominal cramps on 30 November 1969, during the seventh month of pregnancy. Abruptio placentae was diagnosed, and an emergency cesarean section was performed at another hospital. Complete abruption was confirmed at operation and a stillborn fetus was delivered. The blood pressure during operation reached a low of 118/84 mm of mercury (compared with 184/114 on admission). Following the operation the patient was anuric. On the first postoperative day, the serum creatinine was 3.1 mg per 100 ml. The fibrinogen level was normal. On the second day she was transferred to Stanford University Hospital.

On arrival the patient appeared drowsy, but was in no distress. She did not complain of flank pain. The blood pressure was 185/110 mm of mercury. Examination of the fundi revealed A-V nicking and two flame-shaped hemorrhages. Basilar rales, generalized hyperreflexia, and a trace of pedal edema were present. That evening the serum creatinine was 7.4 mg per 100 ml. Prothrombin time, partial thromboplastin time, and fibrinogen level were within normal limits. There was no clot lysis. The platelet count was 65,000 per cu mm and remained depressed for four days. Antinuclear antibodies and lupus enythematosus preparations were negative. The antistreptolysin-O titer was 166 Todd units. By the third postoperative day the serum creatinine had risen to 9 mg per 100 ml. Hemodialysis was instituted. Severe oliguria persisted for three weeks. Although urine output then increased slightly, the patient never recovered an adequate degree of renal function (Chart 1). Several transfusions were required for severe anemia (hematocrit 15 percent) during this stay in hospital.

On the 40th postoperative day she was discharged, and dialysis was continued on an outpatient basis. Nephrotomograms on the 60th day demonstrated that the left kidney was 9.3 cm long and the right kidney 9.5 cm. This represented a 2 cm decrease bilaterally in a period of two months. There was no evidence of calcification.

On the 122nd day the patient was re-admitted for nephrectomy and renal transplantation. The kidney had a thin, granular, knobby cortex. The left kidney was 8.2 cm in its longitudinal axis, the right 8.4 cm. Microscopic examination revealed extensive fibrosis and cortical hyalinization. Approximately 90 percent of the glomeruli were destroyed. The pathological diagnosis was massive cortical necrosis.

On the 138th day a related-donor renal transplantation was performed. Excellent renal function was observed immediately afterward. Sixteen months after transplantation the serum creatinine is 1.0 per 100 ml and the creatinine clearance 71 ml per minute.

Comment

In this case there were certain typical characteristics of massive cortical necrosis, including pro-

longed anuria and oliguria, relative hypotension, severe anemia, and a decrease in kidney size. The irreversible loss of intrinsic renal function was representative of a more common clinical course than was noted in the first two cases.

The pathologic features in the kidneys in this case as in the two others were consistent with Sheehan and Moore's[4] criteria for cortical necrosis and did not resemble those of any other known renal disease.

Discussion

Previous reviews[4,5,8,9] have emphasized that the usual course of renal cortical necrosis with prolonged oliguria is permanent loss of renal function. A second course and then spontaneous recovery of adequate renal function after prolonged oliguria, has been described, but this is an extremely rare event.[1,3,9-11] The patient in the first of the three cases herein reported should be added to the very small number of patients who have regained normal renal function.

A third course, gradual progression to end-stage renal failure after partial recovery of function, is illustrated by the second of the three cases. This course has received no attention in previous reviews,[4,5,8] although it is evident that with increased use of dialysis to support patients throughout their initial period of oliguria, it should occur with increasing frequency.

Earlier reviews[4,5,8] also emphasized adequate renal function as being essential to survival. Cortical necrosis was universally attributed to prolonged, intense vasoconstriction. In animal experiments vasoconstriction had been shown to cause cortical necrosis. Many investigators[16-18] now propose that renal cortical necrosis is the clinical equivalent of the generalized Shwartzman reaction, whereas others feel that the disease results from a combination of the two events.[3] In the Shwartzman reaction the central pathogenic event is disseminated intravascular coagulation, which may result from a wide variety of insults. Many of these, such as neoplasm, overwhelming sepsis, shock or severe trauma, are lethal regardless of their effect on renal function. Others, such as obstetrical complications, carry a relatively good initial prognosis.

Now that hemodialysis and transplantation are generally available, it is clear that eventual recovery of renal function should not be considered the most important prognostic factor in cortical necrosis. Recovery from the event which has precipitated the disseminated intravascular coagulation will determine the fate of the patients.

Since spontaneous recovery of renal function seven weeks after the onset of the disease has been reported,[9,13,19] dialysis for at least two months before resort to nephrectomy is recommended. It has been demonstrated[19] that a small surviving population of juxtamedullary nephrons can gradually undergo adaptive changes which enable them to sustain a remarkable degree of renal function. Since the finding of extensive cortical necrosis on needle biopsy[9,14] does not rule out the survival of such nephrons, the patient should be given opportunity to recover some degree of renal function before nephrectomy is considered.

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